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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,553	07/06/2006	**Jae-Kwan Hwang**	20020-05USA	4188

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EXAMINER	
RAO, SAVITHA M	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,553	HWANG ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 4-5 are pending. Receipt and consideration of Applicants' and remarks/arguments filed on 10/ 22/2010 are acknowledged. Claims 4-5 are under consideration in the instant office action.

Applicants' arguments, filed 10/22/2010, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

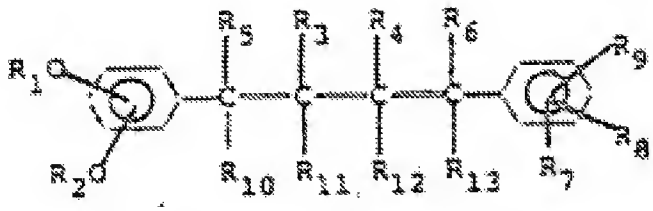
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Rejection of claims 4- 5 under 35 U.S.C. 103(a) as being unpatentable over Neiss (EP 0297733, referenced in the IDS dated 07/06/2006), in view of Deac et al. (abstract only, Igiena (1970), volume 19 (3), pages 167-73), as evidenced by Gibson (Journal of Antimicrobial chemotherapy, 1980, pages 538-570) is maintained for reasons of record restated below.

Neiss teaches pharmaceutical compositions comprising catecholic butane for the treatment of acne (abstract). Neiss additionally teaches that the compounds according to his invention are useful in the treatment of diseases and disorders of the skin, such as acne and psoriasis, and in the healing of skin wounds and breaks in the skin. The compounds also have antibacterial uses (page 2, lines 7-9 and page 4, lines 20-22). Neiss teaches compositions for topical application comprising catecholic butanes of the formula:



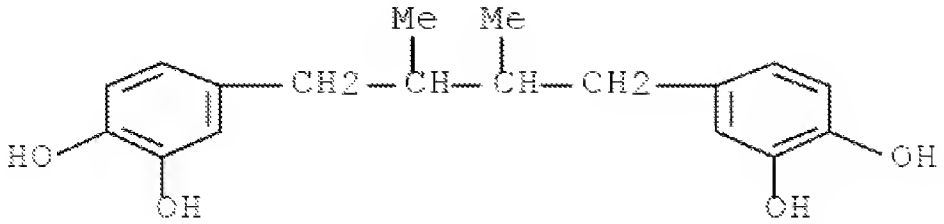
(II)

wherein R_1 and R_2 are independently H, lower alkyl, lower acyl, or alkylene;
R_3, R_4, R_5, R_6, R_{10}, R_{11}, R_{12}, and R_{13} are independently H or lower alkyl;
R_7, R_8 and R_9 are independently H, hydroxy, lower alkoxy, lower acyloxy, or any two adjacent groups together may be alkylene dioxy.

A catecholic butane of formula (II) above, where in R_1, R_3 and R_4 are CH_3, R_2, R_5, R_6, R_9, R_{10}, R_{11}, R_{12} and R_{13} are all hydrogen and R_7 and R_8 together form a alkylene (methylene) dioxy group, is a diastereoisomer of the instantly claimed macelignan (*erythro* {(4-hydorxy,-3-methoxyphenyl)-4-(3,4, methlenedioxyphenyl)-2,3-dimethyl butane}). Neiss teaches the compounds of formula (II) include compounds as a single optical isomer or a racemic mixture of such isomers or distereoisomers (page 5, lines 14-15). As such, Neiss provides an ordinarily skilled artisan motivation to use catecholic butanes, including {(4-hydorxy,-3-methoxyphenyl)-4-(3, 4, methlenedioxyphenyl)-2, 3-dimethyl butane}) and its diastereoisomer, which is the instantly claimed macelignan.

Neiss dose not teach specific inhibition of acne causing bacteria such *propionibacterium acnes, staphylococcus epidermis* and *staphylococcus aureus* as instantly claimed.

However, Deac et al. teaches nordihydroguaiaretic acid (structure shown below) to have a bactericidal effect on *Staphylococcus aureus in vitro*



The compound taught by Deac et al., nordihydroguaiaretic acid, is the preferred compound which has utility in the method of treatment of acne, taught by Neiss et al., where in the catecholic butane encompassed by the of formula (II) of Neiss shown above has in R_1, R_2, R_5, R_6, R_7, R_8 R_9, R_{10}, R_{11}, R_{12} and R_{13} are R_3 and R_4 are CH_3. It is noted that the closer the physical and chemical similarities between the claimed species or subgenus and any exemplary species or subgenus disclosed in the prior art, the greater the expectation that the claimed subject matter will function in an equivalent manner to the genus. See, e.g., *Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904 (and cases cited therein). *Cf. Baird,* 16 F.3d at 382-83, 29 USPQ2d at 1552. As such, Macelignan and its diastereoisomer disclosed as a subgenus of the compounds which also encompasses the compound taught by Deac et al. would also be expected to have antibacterial activity against *S. aureus* similar to the compound taught by Deac et al.

Further, it is well known in the art that acne is caused by bacteria such as *propionibacterium acnes, staphylococcus epidermis* and *staphylococcus aureus*, as evidenced by Gibson (page 2, left column, 1st paragraph). Neiss teaches treatment of acne with compounds structurally similar to the instantly claimed compounds and, as such inhibition of the growth of these bacteria in acne lesions is a functional limitation of the compounds taught by Neiss. It is noted that *In re Best* (195 USPQ 430) and *In re*

Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph). It is also noted that "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). As such, the instantly claimed mechanistic functions of the compounds to inhibit acne-causing bacteria would be present in the identical compounds taught by Neiss and would therefore elicit these effects whenever it is administered for the treatment of acne.

In view of the foregoing references, it would have been *prima facie* obvious to one of ordinary skill in the art to develop a method of treating acne comprising administering to a subject the instantly claimed macelignan. Neiss provides explicit teachings that a compound which is a structural isomer of the instantly claimed macelignan is useful in the treatment of acne, as an antibacterial, and suggests a diastereoisomer of the compounds of his teachings would also have the same utility. Deac et al. teaches nordihydroguaiaretic acid, which is also encompassed by the genus of compounds taught by Neiss, has antibacterial activity against *S. Aureus.* An ordinarily skilled artisan would therefore be motivated to utilize macelignan for treatment

of acne which is characterized by the activity of the bacteria *propionibacterium acnes* and those of staphylococcus species. As such, an ordinarily skilled artisan would have a reasonable expectation of success that macelignan would provide a treatment option for acne.

Response to applicant's arguments filed on 06/04/2010:

Applicant traverses the above rejection with the following arguments:

a. The Neiss '733 genus is too large to obviate a compound that falls within the genus as it encompasses several thousands of compounds. In addition, Neiss does not point to the desirability of using the macelignan compounds and does not exemplify macelignan among the examples of catecholic butanes listed. Neiss focuses on the activities of the compound NDGA which is not a di-oxy cyclic structure as macelignan.

b. Neiss reference internally points away from the claimed invention as it fails to cite compound possessing a di-oxy cyclic phenyl group as a preferred compound or as an example.

c. The function of lignan compounds are conventionally known to be highly sensitive to their structure as demonstrated by Exhibit A (Maruyama et al.) and Exhibit B (Akiyama et al.). Both of which teaches that lignan with similar structures have different antibacterial activity.

d. Cited reference fails to provide enabling disclosure for using macelignan to treat acne as Neiss fails to provide any demonstration of effectiveness of its generic compounds to treat acne.

Applicant's traversal arguments for this rejection have been fully considered, but are not found to be persuasive.

First, it should be noted that the above rejection was made under 35 U.S.C. 103(a) and therefore none of the cited references has to teach every limitation of the instant claims. Applicant is further reminded that the obviousness rejection is not an anticipation rejection. The above mentioned references clearly teach the instantly claimed compound macelignan and the method of utilizing compounds structurally similar to macelignan in the treatment of acne. In obviousness rejection a combination of references is used, and the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references that make up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the combination of the cited references. *In re Young*, 403 F.2d 754, 159 USPQ 725(CCPA 1968); *In re Keller 642 F.2d 413, 208 USPQ 871 (CCPA 1981).*

In response to applicant's argument that Neiss '733 genus is too large to obviate a compound that falls within the genus as it encompasses several thousands of compound and that Neiss does not point to the desirability of using the macelignan compounds and does not exemplify macelignan among the examples of catecholic

butanes listed. Examiner would like to point out that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious". KSR v. Teleflex, 127 S,Ct. 1727, 1740 (2007)(quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is... a person of ordinary creativity, not an automaton." Id. at 1742. In the instant case, Neiss explicitly teaches and claims a diastereoisomer of mace lignan as being encompassed by the genus of catecholic butane of formula (II) above, where in R_1, R_3 and R_4 are CH_3, R_2, R_5, R_6, R_9, R_{10}, R_{11}, R_{12} and R_{13} are all hydrogen and R_7 and R_8 together form a alkylene (methylene) dioxy group. **Neiss also teaches that it will be appreciated by those skilled in the art that their Formula II is directed to both the phenolics compounds and the conventional esters and ethers thereof**. The genus of compounds taught by Neiss has a large unchanging parental structural nucleus and is expressly taught to have several utilities which also include treatment of acne. This utility of compounds claimed by Neiss is further

ascertained by Deac et al. who teach the utility of one of the compounds encompassed by the genus taught by Neiss to be useful in the treatment of acne which has bactericidal effect on staphylococcus aureus. In this instance each compounds encompassed by the generic formula is disclosed as having a substantially same utility. Consistent with this reasoning, it would have obvious for an ordinarily skilled artisan to utilize different compounds and their isomers, compounds taught by Neiss in the various methods of treatment suggested by Neiss to arrive at the instantly claimed method "yielding no more than one would expect from such an arrangement".

In response to applicant's argument that Neiss reference internally points away from the claimed invention, as it fails to cite compound possessing a di-oxy cyclic phenyl group as a preferred compound or as an example, Examiner finds this unpersuasive since Neiss explicitly teaches and claims his generic compounds to encompass the alkylene dioxy substitution and specifically recites that one of ordinary skill would be able to appreciate the conventional esters and ethers associated with their generic compound. It is noted that a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989).

In response to the applicant's argument that the function of lignan compounds are conventionally known to be highly sensitive to their structure as demonstrated by Exhibit A (Maruyama et al.) and Exhibit B (Akiyama et al.), Examiner while considering the two exhibits presented finds them unpersuasive. While the examiner agrees with the

applicants that the cited exhibits show that the lignans with similar structures could have different antibacterial activity, it is noted that only upon testing was it discovered that one isomer had activity while the other did not or certain modification to the structure resulted in the disappearance of antibacterial activity. Neither of these references is drawn to the catechol butanes or macelignan instantly claimed. While the references may suggest to an ordinarily skilled artisan that different lignan compounds closely related structurally, may not have the same activity, the do not dissuade an ordinarily skilled artisan to test the structurally related lignan compounds for utility (in this instant activity against acne) which is suggested in the prior art. In fact the references motivate an ordinarily skilled artisan to conduct a thorough structural activity relationship studies among compounds that have similar structure to determine the active analogs of the same.

In response to applicants argument that the cited reference fails to provide enabling disclosure for using macelignan to treat acne as Neiss fails to provide any demonstration of effectiveness of its generic compounds to treat acne, it is noted that the "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10

USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). In this instance Neiss explicitly teaches the utility of compounds encompassed by his generic formula II in the treatment of acne which would suggest and motivate one having ordinary skill in the art to utilize or test these compounds for that activity.

Accordingly, the arguments set forth by the applicants are unpersuasive and the rejection is maintained.

Conclusion

Claims 4-5 are rejected. No claims are allowed

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7.00 am to 4.00 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAVITHA RAO/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614